

**Prescribing Information** - Please refer to the Summary of Product Characteristics (SmPC) before prescribing.

**Metoject® PEN (methotrexate) 7.5 mg / 10 mg / 12.5 mg / 15 mg / 17.5 mg / 20 mg / 22.5 mg/ 25 mg/ 27.5 mg / 30 mg solution for injection in pre-filled pen**

**Qualitative and quantitative composition:** 1 pre-filled pen with 0.15 ml (0.20 ml; 0.25 ml; 0.30 ml; 0.35 ml; 0.40 ml; 0.45 ml; 0.50 ml; 0.55 ml; 0.60 ml) contains 7.5 mg (10 mg; 12.5 mg; 15 mg; 17.5 mg; 20 mg; 22.5 mg; 25 mg; 27.5 mg; 30 mg) methotrexate. **Excipients:** NaCl, NaOH, HCl, water for injections. **Therapeutic indications:** Active rheumatoid arthritis in adult patients; polyarthritic forms of severe, active juvenile idiopathic arthritis, when the response to nonsteroidal anti-inflammatory drugs (NSAIDs) has been inadequate; moderate to severe psoriasis in adult patients who are candidates for systemic therapy, and severe psoriatic arthritis in adults; mild to moderate Crohn's disease either alone or in combination with corticosteroids in adult patients refractory or intolerant to thiopurines. **Posology and method of administration:** Should only be prescribed by physicians who are familiar with the various characteristics of the medicinal product and its mode of action. Patients must be educated to use the proper injection technique. The first injection of Metoject PEN should be performed under direct medical supervision. **Adults, rheumatoid arthritis:** The recommended initial dose is 7.5 mg of Metoject once weekly, administered subcutaneously. Depending on the individual activity of the disease and tolerability, the dose may be increased gradually by 2.5 mg per week. A weekly dose of 25 mg should in general not be exceeded. **Polyarthritic forms of juvenile idiopathic arthritis:** The recommended dose is 10-15 mg/m<sup>2</sup> body surface area (BSA)/once weekly, administered subcutaneously. In therapy-refractory cases the weekly dosage may be increased up to 20 mg/m<sup>2</sup> BSA/once weekly. Use in children < 3 years of age is not recommended as insufficient data on efficacy and safety is available for this population. **Psoriasis vulgaris, psoriatic arthritis:** Test dose of 5 – 10 mg should be administered parenterally, one week prior to therapy to detect idiosyncratic adverse reactions. The recommended initial dose is 7.5 mg of methotrexate once weekly, administered subcutaneously. The dose is to be increased gradually but should not, in general, exceed a weekly dose of 25 mg of methotrexate. **Crohn's disease:** Induction treatment: 25 mg/week administered subcutaneously. Response to treatment can be expected after approximately 8 -12 weeks. Maintenance treatment: 15 mg/week. **Elderly:** Dose reduction should be considered due to reduced liver and kidney function as well as lower folate reserves. If changing the oral to parenteral administration a reduction of dose may be required due to the variable bioavailability. **Contraindications:** Hypersensitivity to methotrexate or any of the excipients; severe liver impairment; alcohol abuse; severe renal impairment (creatinine clearance < 30 ml/min); pre-existing blood dyscrasias (bone marrow hypoplasia, leukopenia, thrombocytopenia, significant anaemia); serious, acute or chronic infections such as tuberculosis, HIV, other immunodeficiency syndromes; ulcers of the oral cavity and known active gastrointestinal ulcer disease; pregnancy, breastfeeding; concurrent vaccination with live vaccines. **Special warnings and precautions for use:** In the treatment of rheumatoid arthritis, juvenile idiopathic arthritis, psoriasis and psoriatic arthritis, and Crohn's disease, Metoject PEN (methotrexate) must only be used once a week. Dosage errors in the use can result in serious adverse reactions, including death. **Undesirable effects:** Most serious adverse reactions of methotrexate include bone marrow suppression, pulmonary toxicity, hepatotoxicity, renal toxicity, neurotoxicity, thromboembolic events, anaphylactic shock and Stevens-Johnson syndrome. Most frequently (very common) observed adverse reactions of methotrexate include gastrointestinal disorders e.g. stomatitis, dyspepsia, abdominal pain, nausea, loss of appetite and abnormal liver function tests e.g. increased ALAT, ASAT, bilirubin, alkaline phosphatase. Other frequently (common) occurring adverse reactions are leukopenia, anaemia, thrombopenia, headache, tiredness, drowsiness, pneumonia, interstitial alveolitis/pneumonitis often associated with eosinophilia, oral ulcers, diarrhoea, exanthema, erythema and

pruritus. **Effects:** Pharyngitis, infection (incl. reactivation of inactive chronic infection), sepsis, conjunctivitis. Lymphoma. Leukopenia, anaemia, thrombopenia, pancytopenia, agranulocytosis, severe courses of bone marrow depression, lymphoproliferative disorders, eosinophilia. Allergic reactions, anaphylactic shock, hypogammaglobulinaemia. Precipitation of diabetes mellitus. Depression, confusion, mood alterations. Headache, tiredness, drowsiness, dizziness, pain, muscular asthenia or paraesthesia/ hypoesthesia, changes in sense of taste (metallic taste), convulsions, meningism, acute aseptic meningitis, paralysis, encephalopathy/ leukoencephalopathy. Visual disturbances, impaired vision, retinopathy. Pericarditis, pericardial effusion, pericardial tamponade. Hypotension, thromboembolic events. Pneumonia, interstitial alveolitis/pneumonitis often associated with eosinophilia. Symptoms indicating potentially severe lung injury (interstitial pneumonitis) are: dry, not productive cough, short of breath and fever, pulmonary fibrosis, Pneumocystis jirovecii pneumonia, shortness of breath and bronchial asthma, pleural effusion, epistaxis, pulmonary alveolar haemorrhage. Stomatitis, dyspepsia, nausea, loss of appetite, abdominal pain, oral ulcers, diarrhoea, gastrointestinal ulcers and bleeding, enteritis, vomiting, pancreatitis, gingivitis, haematemesis, haematemesis, toxic megacolon. Abnormal liver function tests (increased ALAT, ASAT, alkaline phosphatase and bilirubin), cirrhosis, fibrosis and fatty degeneration of the liver, decrease in serum albumin, acute hepatitis, hepatic failure. Exanthema, erythema, pruritus, photosensitisation, loss of hair, increase in rheumatic nodules, skin ulcer, herpes zoster, vasculitis, herpeticiform eruptions of the skin, urticarial, increased pigmentation, acne, petechiae, ecchymosis, allergic vasculitis, Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell's syndrome), increased pigmentary changes of the nails, acute paronychia, furunculosis, telangiectasia, skin exfoliation/ dermatitis exfoliative. Arthralgia, myalgia, osteoporosis, stress fracture, osteonecrosis of jaw (secondary to lymphoproliferative disorders). Inflammation and ulceration of the urinary bladder, renal impairment, disturbed micturition, renal failure, oliguria, anuria, electrolyte disturbances, proteinuria. Inflammation and ulceration of the vagina, loss of libido, impotence, gynaecomastia, oligospermia, impaired menstruation, vaginal discharge. Fever, wound-healing impairment, asthenia, injection site necrosis, oedema. Subcutaneous application of methotrexate is locally well tolerated. Only mild local skin reactions (such as burning sensations, erythema, swelling, discolouration, pruritus, severe itching, pain) were observed, decreasing during therapy. **Overdose:** Calcium folinate is the specific antidote for neutralising the toxic undesirable effects of methotrexate.

**Basic NHS price:**

7.5 mg/0.15 ml single pen	£12.87
10 mg/0.20 ml single pen	£13.26
12.5 mg/0.25 ml single pen	£14.35
15 mg/0.30 ml single pen	£14.41
17.5 mg/0.35 ml single pen	£15.25
20 mg/0.40 ml single pen	£15.56
22.5 mg/0.45 ml single pen	£16.11
25 mg/0.50 ml single pen	£16.13
27.5 mg/0.55 ml single pen	£16.50
30 mg/0.60 ml single pen	£16.56

**Legal classification:** POM

**Marketing authorisation holder:** medac GmbH, Theaterstr. 6, 22880 Wedel, Germany.

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**Marketing authorisation number:** PL 11587/0076 - 0085

**Date of revision of text:** 09.2023

**Website:** [www.metoject.co.uk](http://www.metoject.co.uk)

Adverse events should be reported. Reporting forms and information can be found at [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard). Adverse events should also be reported to medac drug safety at: [drugsafety@medac.de](mailto:drugsafety@medac.de)